CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

DIFENACOUM

Chemical Code # 5942, **Tolerance #** 53007
SB 950 # New A.I.

10/13/06

I. DATA GAP STATUS

Chronic toxicity, rat:	No study submitted; not required at this time.
Chronic toxicity, dog:	No study submitted; not required at this time.
Oncogenicity, rat:	No study submitted; not required at this time.
Oncogenicity, mouse:	No study submitted; not required at this time.
Reproduction, rat:	No study submitted; not required at this time.
Teratology, rat:	Study acceptable; no adverse effect indicated.
Teratology, rabbit:	Study acceptable; no adverse effect indicated.
Gene mutation:	Study acceptable; no adverse effect indicated.
Chromosome effects:	Study acceptable; possible adverse effect.
DNA damage:	Study acceptable; no adverse effect indicated.
Neurotoxicity:	No study submitted; not required at this time.

Toxicology one-liners are attached.

All record numbers through 224954 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
indicates a study on file but not yet reviewed.
File name: T061013
Revised by T. Moore, 10/13/06

Note: the active ingredient is a rodenticide which is specified for a non-food use.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

No study submitted; not required at this time.

CHRONIC TOXICITY, RAT

No study submitted; not required at this time.

CHRONIC TOXICITY, DOG

No study submitted; not required at this time.

ONCOGENICITY, RAT

No study submitted; not required at this time.

ONCOGENICITY, MOUSE

No study submitted; not required at this time.

REPRODUCTION, RAT

No study submitted; not required at this time.

TERATOLOGY, RAT

0010, 224941; "Difenacoum: Developmental Toxicity Study in the Rat" (Hodge, M.C.E., Zeneca Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK, Report No. CTL/P/4354, 06/26/94). 833. Difenacoum Technical (Batch no. BX 0009, purity = 98.5%), mixed in polyethylene glycol (PEG 300), was administered as a single daily dose by gavage to 24 pregnant Alpk:APfSD (Wistar-derived) rats per dose at dose levels 0 (vehicle only), 0.01, 0.03, or 0.09 mg/kg/day from gestation day 7 through gestation day 16 (inclusive). One dam at 0.01 mg/kg/day and seven dams at 0.09 mg/kg/day were sacrificed for humane reasons on day 7 and on day 16, respectively. Treatment-related paleness, subdued behavior, colored feces, and vaginal bleeding were observed in dams at 0.09 mg/kg/day. A treatment-related increase in mean kaolin-cephalin time in dams at 0.09 mg/kg/day was observed. No treatment-related effects on body weight or food consumption were observed. Macroscopic examination of the dams that were sacrificed at 0.09 mg/kg/day revealed pale liver, lungs, and pancreas, contents of stomach discolored (red/brown), contents of uterus discolored (red/brown), and blood in the lumen of the vagina. Analyses of mean fetal weight, mean number of fetuses per animal, and the mean number of resorptions per animal revealed no treatment-related effects. No treatment-related fetal abnormalities were observed. **Possible adverse effect: internal hemorrhaging in dams. Maternal NOEL =** 0.03 mg/kg/day (based on signs of internal hemorrhaging), **Developmental NOEL =** 0.09 mg/kg/day (based on no effects at the highest dose tested). **Acceptable.** (Corlett and Leung, 09/01/06)

TERATOLOGY, RABBIT

0010, 224942; "Difenacoum: Developmental Toxicity Study in the Rabbit" (Hodge, M.C.E., Zeneca Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK, Report No. CTL/P/4245, 07/07/94). 833. Difenacoum Technical (Batch no. BX 009, purity = 98.5%), mixed in polyethylene glycol 300 (PEG 300), was administered as a single daily dose by gavage to 20 pregnant New Zealand White rabbits per dose at dose levels 0 (vehicle only), 0.001, 0.005, or 0.015 mg/kg/day from gestation day 8 through gestation day 20 (inclusive). 12 dams were sacrificed at 0.015 mg/kg/day between days 16 and 20, 11 for humane grounds (because the coagulation times exceeded set criteria) and 1 following abortion. No treatment-related clinical signs were observed. Treatment-related increases in mean prothrombin and mean

kaolin-cephalin times in dams at 0.015 mg/kg/day were observed. No treatment-related effects on body weight or food consumption were observed. Macroscopic examination of the dams at 0.015 mg/kg/day that were sacrificed intercurrently revealed mottled lungs and stomachs with sloughed mucosa (glandular). Analyses of mean fetal weight, mean number of fetuses per animal, and the mean number of resorptions per animal revealed no treatment-related effects. No treatment-related fetal abnormalities were observed. **Possible adverse effect: internal hemorrhaging in dams. Maternal NOEL =** 0.005 mg/kg/day (based on signs of internal hemorrhaging), **Developmental NOEL =** 0.015 mg/kg/day (based on no effects at the highest dose tested). **Acceptable.** (Corlett and Leung, 09/12/06)

GENE MUTATION

** 53007-0011; 224943; "Difenacoum: Reverse Mutation in 5 Histidine-Requiring Strains of *Salmonella typhimurium*"; (M. Ballantyne; Hazleton Europe Limited, North Yorkshire HG3 1PY, England; Report No. 355/22-1052; 6/26/95); *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA102 were treated with Difenacoum technical (batch no. 0001, purity: 98.7%) at concentrations ranging from 8 to 5000 μg/ml for 72 hours at 37° C under conditions of +/- activation in the 1st trial using the plate incorporation technique. In the 2nd trial, the strains were exposed to concentrations of the test material ranging from 250 to 4000 ug/plate under conditions of activation and from 312.5 to 5000 ug/plate, preincubating the cells for 1 hour followed by plating the cells. Each treatment level was plated in triplicate. An Aroclor 1254-induced rat liver S9 fraction was used to activate the test material. There was no apparent treatment-related increase in the incidence of reverse mutation. The positive controls were functional (note: under conditions of activation, no positive control for the TA1535 and TA102 were employed); **No adverse effect indicated. Study acceptable.** (Moore, 9/25/06)

** 53007-0011; 224944; "Difenacoum - An Evaluation in the *Salmonella* Mutagenicity Assay"; (R.D. Callander; Imperial Chemical Industries PLC, Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK; Report No. CTL/P/1448; 3/3/86); *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were treated with Difenacoum technical (batch ref. no. RS 272/C, purity: 96.8%) at concentrations ranging from 1.6 to 5000 μg/plate for 64 to 68 hours at 37° C under conditions of +/- activation in two trials, using the plate incorporation technique. Each treatment level was plated in triplicate. An Aroclor 1254-induced rat liver S9 fraction was used to activate the test material. There was no apparent treatment-related increase in the incidence of reverse mutation. The positive controls were functional; **No adverse effect indicated. Study acceptable.** (Moore, 9/25/06)

** 53007-0012; 224947; "Difenacoum: Mutation at the Thymidine Kinase (tk) Locus of Mouse Lymphoma L5178Y Cells using the Microtitre Fluctuation Technique"; (J. Clements; Corning Hazleton (Europe), North Yorkshire HG3 1PY, England; Report No. 355/16-1052; 6/12/95); Mouse lymphoma L5178Y cells were treated with Difenacoum technical (batch no. 0001; purity: 98.7%) at concentrations ranging from 3.125 to 100 ug/ml under conditions of both non-activation under conditions of activation for 3 hours at 37° C in the first trial. In the second trial, the cells were exposed to concentrations ranging from 40 to 80 ug/ml. Duplicate cultures/treatment level were included in the study. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. Cell survival and viability and mutation frequency for each treatment level were determined and compared to those of the solvent control. In the 1st trial, the 75 ug/ml treatment level In the non-activated assay demonstrated an increased mutation frequency ($p<0.05$). However, this effect was not evident in the 2nd trial. For the assays with the S9 fraction, there was no dose-related increase in mutation frequency. Positive controls were functional. **No adverse effect indicated. Study acceptable.** (Moore, 10/2/06)

CHROMOSOME EFFECTS

**** 53007-0011; 224945**; "Difenacoum: Induction of Chromosome Aberrations in Cultured Human Peripheral Blood Lymphocytes"; (S. Riley; Corning Hazleton (Europe), North Yorkshire HG3 1PY, England; Report No. 355/21-1052; 6/13/95); Human lymphocytes (whole blood) were treated with Difenacoum technical (batch no. 0001, purity: 98.7%) at concentrations ranging from 8.898 to 450 ug/ml in the 1st trial and 75.5 to 450 ug/ml in the 2nd trial under conditions of activation and from 15.83 to 184.3 ug/ml under conditions of non-activation at 37° C. Under conditions of activation, the cells were exposed to the test material for 3 hours, washed and then incubated for an additional 17 hours (1st trial) and 17 or 41 hours (2nd trial). In the non-activated assays, the cells were exposed to the test material for 20 hours (1st trial) and 20 or 44 hours (2nd trial). A liver homogenate S9 fraction from male rats pretreated with Aroclor 1254 was used to metabolize the test material. Under conditions of activation, an increased number of cells exhibited chromosomal aberrations in a dose-related manner. **Possible adverse effect:** increased numbers of cells exhibiting chromosomal aberrations when activated. The positive controls were functional for both activation and non-activation. **Study acceptable.** (Moore, 9/28/06)

**** 53007-0011; 224946**; "Difenacoum - An *In Vitro* Cytogenetic Study in Chinese Hamster Lung Fibroblasts"; (J. Wildgoose, C.A. Howard, P. Clay, C.R. Richardson; Imperial Chemical Industries PLC, Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK; Report No. CTL/P/1553; 11/3/86); Chinese Hamster lung fibroblasts were treated with Difenacoum technical (batch no. 4134 3712/0108; purity: 96.8%) at concentrations ranging from 1 to 100 ug/ml for 3 hours followed by an additional incubation period for either 9 or 21 hours. Treatments were performed with or w/o activation with duplicate samples for each treatment level. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. At 2 hours prior to harvest, colchicine (10 ug/ml) was added to arrest the dividing cells in metaphase. An increased number of cells with chromosomal aberrations was noted both under conditions of activation or non-activation after 12 and/or 24 hours of incubation. **Adverse effect:** increased number of cells with chromosomal aberrations; the positive controls were functional. **Study acceptable.** (Moore, 9/29/06)

DNA DAMAGE

** 53007-0012; 224948; "Difenacoum: Induction of Micronuclei in the Bone Marrow of Treated Rats"; (S. Riley; Corning Hazleton (Europe), North Yorkshire HG3 1PY, England; Report No. 355/37-1052; 6/4/95); Ten Sprague-Dawley rats/sex/group were dosed orally by gavage with 0 (vehicle: corn oil), 500, 1000 or 2000 mg/kg of Difenacoum technical (batch no. 0040, purity: 94.6%). Five animals/sex/time point were euthanized at 24 and 48 hours post-dose. In addition, 5 animals/sex were dosed with 80 mg/kg of cyclophosphamide (positive control) and euthanized at 24 hours post-dose. Bone marrow samples from the femurs of each animal were examined and 2000 polychromatic erythrocytes (PCE) per animal were examined for micronuclei. The ratio of PCE's to normochromatic erythrocytes (PCEs/NCE) was calculated as well. There was no treatment-related increase in the number of PCE's with a micronucleus. **No adverse effect indicated.** The positive control was functional. **Study acceptable.** (Moore, 10/2/06)

** 53007-0012; 224949; "Difenacoum: An Evaluation in the Mouse Micronucleus Test"; (T. Sheldon, C.R. Richardson, V. Randall, D. Hart; Imperial Chemical Industries PLC, Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK; Report No. CTL/P/1666; 7/20/87); Fifteen C57BL/6J/Alpk mice/sex/group were dosed orally by gavage with 0 (vehicle: corn oil), 3125 or 5000 mg/kg of Difenacoum technical (reference no. Y00441/004/012, purity: 96.8%). A positive control group of 15 animals/sex were dosed orally by gavage with 65 mg/kg. Five animals/sex/time point were euthanized at 24, 48, and 72 hours post-dose. Bone marrow samples from the femurs of each animal were examined and 1000 polychromatic erythrocytes (PCE) per animal were examined for micronuclei. The percentage of PCE's in the total erythrocyte population was determined as well. There was no treatment-related increase in the number of PCE's with a micronucleus. **No adverse effect indicated.** The positive control was functional. **Study acceptable.** (Moore, 10/3/06)

** 53007-0012; 224950; "Difenacoum: Measurement of Unscheduled DNA Synthesis in Rat Liver Using an *In Vivo/In Vitro* Procedure"; (C. Clare; Corning Hazleton (Europe), North Yorkshire HG3 1PY, England; Report No. 355/38-1052; 6/14/06); Five male rats/group/time point were dosed with 0 (corn oil), 800 or 2000 mg/kg of S-1283 technical (batch no. 931027AMG, purity: 95.3%) and euthanized 2 to 4 hours or 12 to 14 hours after dosing. As positive controls, 5 males/group were treated with 75 mg/kg of 2-acetamidofluorene and euthanized 12 to 14 hours after dosing or 10 mg/kg of dimethynitrosamine and euthanized 2 to 4 hours post-dose. Upon recovery of the hepatocytes, a primary culture was established and the cells were exposed to ^{3}H-thymidine (10 uCi/ml) for 4 hours, followed by further incubation overnight with unlabeled thymidine. Two cultures/animal in each trial, 50 cells/culture, were evaluated for the number of net grains/nucleus. There was no treatment-related increase in unscheduled DNA synthesis. The positive controls were functional. **No adverse effect indicated. Study acceptable.** (Moore, 10/3/06)

** 53007-0012; 224951; "Difenacoum: Assessment for the Induction of Unscheduled DNA Synthesis in Rat Hepatocytes *In Vivo*"; (J.C. Kennelly; Imperial Chemical Industries PLC, Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK; Report No. CTL/P/3017; 6/4/90); Five male Alpk:APfSD rats/group/time point were dosed orally by gavage with 250, 500 or 1000 mg/kg of Difenacoum Technical (batch no. 0005; purity: 92.5%) and euthanized at 4 or 12 hours after dosing. Only the animals in the 500 and 1000 mg/kg groups were processed for the UDS assessment. Two animals in the positive control group were treated with 40 mg/kg of 6-p-dimethylaminophenylazobenzthiazole (6BT) and euthanized 12 hours after dosing. An additional 2 animals were treated orally by gavage with 10 mg/kg of N-nitrosodimethylamine (NDMA) and euthanized at 4 hours post-dose. Upon recovery of the hepatocytes, a primary culture was established and the cells were exposed to ^{3}H-thymidine for 4 hours, followed by further incubation overnight with unlabeled thymidine. Two cultures/animal in each trial, 50 cells/culture, were evaluated for the number of net grains/nucleus. There was no treatment-related increase in unscheduled DNA synthesis. The positive controls were functional. **No adverse effect indicated. Study acceptable.** (Moore, 10/4/06)

NEUROTOXICITY

No study submitted; not required at this time.

SUBCHRONIC STUDIES

Rat Subchronic Oral Toxicity Study

0009, 224937; "Difenacoum: Oral Toxicity Study in Rats" (Horner, J.M., ICI Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK, Report No.: CTL/P/3504, 11/29/91). Difenacoum (Batch no. 0009, purity = 97.0%) was mixed in polyethylene glycol 300 (PEG 300) and administered once daily by gavage to 5 or 10 Crl:CD(SD)BR (Sprague-Dawley derived) rats per sex per dose at levels of 0 (vehicle only) (10), 0.01(5), 0.02/0.09 (5), or 0.03 (10) mg/kg/day for 29 to 93 days. On day 29, 5 satellite males at both 0 and 0.03 mg/kg/day dose levels were sacrificed and blood clotting times were determined. On day 33, 3 satellite females at both 0 and 0.03 mg/kg/day dose levels were sacrificed and blood clotting times were determined and on day 36, 2 additional satellite females at both 0 and 0.03 mg/kg/day dose levels were sacrificed and blood clotting times were determined. Starting at day 65 for females and at day 66 for males, the dose level of the 0.02 mg/kg/day group was increased to 0.09 mg/kg/day with 2 males at this dose level dying on days 72 and 73 and the remaining 3 males sacrificed on day 74, and with 2 females at this dose level dying on days 81 and 89 and the remaining 3 females sacrificed on day 89. On day 77, 1 male at 0.03 mg/kg died; the surviving males at 0, 0.01, and 0.03 mg/kg/day were sacrificed on day 78. The surviving females at 0, 0.01, and 0.03 mg/kg/day were sacrificed on day 93. Treatment-related salivation was observed in both sexes (main group) at all dose levels and treatment-related diarrhea was observed in males at 0.02/0.09 and 0.03 mg/kg/day (main group). No treatment-related effects on mean clotting indices (prothrombin and kaolin-cephalin) were observed in the satellite animals. Markedly increased mean clotting time indices were observed at 0.02/0.09 mg/kg/day in both sexes. Also at

0.02/0.09 mg/kg/day, a treatment-related decrease in mean hematocrit level and an increase mean neutrophil level were observed. Macroscopic examination of animals of both sexes at 0.02/0.09 mg/kg/day revealed hemorrhage and red discoloration of various internal organs and microscopic examination of these tissues revealed hemorrhage. No treatment-related macroscopic and microscopic abnormalities were observed in males and females at 0.01 mg/kg/day and in females at 0.03 mg/kg/day (main group). **Possible adverse effect indicated: internal hemorrhaging.** NOEL (M/F) < 0.01 mg/kg/day based on treatment-related salivation observed at all dose levels. **Supplemental study** (only 5 animals per sex per dose level were used and no ophthalmological examinations were conducted). (Corlett, 08/17/06)

Dog 6-Week Oral Toxicity Study

0009, 224938; "6 Week Oral Toxicity Study in Dogs" (Hodge, M.C.E., Zeneca Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK, Report No.: CTL/L/5738, 03/29/94). Difenacoum (Batch no. BX 009, purity = 98.5%) was formulated in polyethylene glycol 300 (PEG 300) and administered orally via gelatin capsules to 1 beagle dog per sex per dose at levels of 0 (capsules containing vehicle only), 0.01, 0.025, 0.05, 0.1, or 0.2 mg/kg/day for up to 6 weeks. Animals dosed with 0.025, 0.05, 0.1, and 0.2 mg/kg/day were sacrificed for humane reasons on weeks 3, 2, 2, and 1, respectively; in some instances, pallor of the mucus membranes, general pallor, reduced activity, subdued behavior, and/or coldness were observed. The onset of pallor was very rapid. At 0.01 mg/kg/day, treatment-related increases in prothrombin time (starting on day 30) and kaolin- cephalin time (starting on day 37) were observed in both sexes. No effects on blood clinical chemistry or cytology were observed. **Possible adverse effect indicated: internal hemorrhaging.** NOEL (M/F) < 0.01 mg/kg/day based on treatment-related increases in coagulation times at all dose levels. **Supplemental study** (only 1 animal per sex per dose level was used, the animals were only dosed up to 6 weeks, and no ophthalmological examinations were conducted). (Corlett, 08/21/06)

METABOLISM STUDIES

Metabolism, Rat

53007-0013; 224952; "Difenacoum: Elimination from the Tissues of Rats Following Administration of a Single Oral Dose"; (H. Bratt; Imperial Chemical Industries PLC, Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK; Report No. CTL/P/1592; 4/10/87); Thirty two male Alpk:AP rats were dosed orally by gavage with 1.2 mg/kg of ^{14}C-labeled-Difenacoum (phenyl-ring of coumarin moiety) (specific activity: 1961 Mbq/mmole; radiochemical purity: 93.1%, cis:trans ratio: 44:56). Three animals per time point were euthanized at 1, 4 and 8 days and 2, 4, 8, 12 and 26 weeks after dosing. Blood was collected by cardiac puncture and the liver, kidneys, pancreas, salivary glands and a sample of abdominal fat were removed for radioanalysis. The prothrombin time and kaolin-cephalin time were measured for each blood sample. The liver was the primary tissue in which the radiolabel was isolated. Forty one percent of the administered dose was recovered from the organ 24 hours after dosing. Even 6 months after dosing, 3% of the administered dose was still present in the liver. A biphasic elimination process was noted with a half-life for the rapid phase being 3 days and a half-life of the slow phase of 118 days. The cis isomer of the active ingredient demonstrated a longer residence time in the liver. By 14 days, the trans form was no longer detectable. Other metabolites were also isolated in the liver, but were not chemically identified in the study. The kaolin-cephalin clotting time for the blood was affected for up to 4 days post-dose. The prothrombin measure of clotting time was apparently more severely affected at 24 hours post-dose, recovering more quickly by 4 days. **Study supplemental** (the study did not fulfill guideline requirements). (Moore, 10/11/06)

53007-0013; 224953; " An Investigation into the Elimination and Tissue Distribution of the ^{14}C-Labelled Stereoisomers of Difenacoum Following Oral Administration in Rats"; (J.C. Phillips; TNO BIBRA International Ltd, Carshalton, Surrey SM5 4DS, UK; Report No. 3175/3/02; 1/22/02); Four female Sprague-Dawley rats/group were dosed orally by gavage with 0.5 mg/kg of either cis- [^{14}C-hydroxycoumarin] Difenacoum (purity: 94.4%) or trans-[^{14}C-hydroxycoumarin] Difenacoum (purity: 94.5%). The purified isomers were isolated by thin layer chromatography from [^{14}C-

hydroxycoumarin] Difenacoum (radiochemical purity: >97%, specific activity: 58.4 mCi/mmole, cis/trans isomer ratio: 52/48). Urine and feces samples were collected for 4 days. Blood samples were drawn from the tail vein at 1, 2, 4, 8, 24 and 96 hours post-dose. The radiolabel was primarily excreted in the feces with 41% and 44% of the administered dose recovered via this pathway in the cis and trans-isomer treatment groups, respectively. Blood levels of radiolabel peaked at 8 hours post-dose for both groups. The peak concentration of the radiolabel in the cis-isomer treatment group was approximately 2.5 times that of the trans-isomer treated group (212 ng equivalents of difenacoum/g vs. 83 ng equivalents of difenacoum/g). At 4 days post-dose, 42 and 44% of the administered radiolabel was recovered in the tissues of the cis- and trans-isomer treatment groups, respectively, primarily in the liver (21 and 26%, respectively). **Study supplemental** (the study did not fulfill guideline requirements). (Moore, 10/10/06)

53007-0013; 224954; "An Investigation into the Absorption, Tissue Distribution and Elimination of the ^{14}C-Labelled Difenacoum Following Oral Administration to Rats"; (J.C. Phillips; BIBRA International, Carshalton, Surrey, SM5 4DS, UK; Report No. 1555/2/2/96); Four female Sprague-Dawley rats/group were dosed orally by gavage with 0.05 or 0.5 mg/kg of [^{14}C-hydroxycoumarin] Difenacoum (radiochemical purity: >97%, specific activity: 58.4 mCi/mmole; cis/trans isomer ratio: 52/48). Urine and feces samples were collected for 7 days. Carbon dioxide sampling was performed for the first 24 hours post-dose. Blood samples were drawn during the first 24 hours as well. The radiolabel was primarily excreted in the feces with 39% and 51% of the administered dose recovered via this pathway in the 0.05 and 0.5 mg/kg groups, respectively. Only 0.36 and 1.85% of the radiolabel was recovered in the exhaled carbon dioxide and urine, respectively, of the 0.05 mg/kg group. In the 0.5 mg/kg group, 0.06 and 1.43% of the administered radiolabel was recovered in the carbon dioxide and urine, respectively. Blood levels of radiolabel peaked at 4 hours post-dose for the 0.05 mg/kg group and at 8 hours post-dose for the 0.5 mg/kg group. At 7 days post-dose, 62 and 39% of the administered radiolabel was recovered in the tissues of the 0.05 and 0.5 mg/kg groups, respectively, primarily in the liver (37 and 21%, respectively). Analysis of the chemical moieties recovered in the feces revealed that 37 and 43% of the recovered radiolabel was the unmetabolized parent compound for the 0.05 and 0.5 mg/kg groups, respectively. The other chemical moieties which were isolated were not identified. In the liver, 64 and 47% of the recovered radiolabel was the parent compound for the 0.05 and 0.5 mg/kg groups, respectively. The long term retention of the active ingredient in the liver is the unique aspect of this chemical. **Study supplemental** (the study did not fulfill guideline requirements). (Moore, 10/6/06)